DETAILED ACTION

The examiner, SPE Woitach, and applicant's representative, Viola Kung, participated in an interview on 7/10/2009. As a result of this interview, the examiner agreed to more thoroughly search the art for (1) an indication that heparin binding is not required for AAV-2 cardiac tropism or (2) abolishing AAV-2 tropism for liver, while maintaining AAV-2 tropism for heart is related to abolishment of heparin binding.

RESPONSE TO ARGUMENTS

35 USC § 103

The rejection of claims 11, 16-18 and 20 under 35 U.S.C. 103(a) as being unpatentable over Warrington et al. (US2006/0088936, published 27 April 2006) in view of Bartlett et al. (US Patent 6,962,815, issued 8 November 2005) and further in view of Kaplitt et al. (US Patent, 6,162,796, issued 19 December 2000) and further in view of Wu Xiao (PhD Dissertation 2002, University of Florida) is withdrawn in response to the applicants arguments and/or claim amendments.

The applicant's arguments have been fully considered and are persuasive.

As a result of the interview of 7/10/2009 and subsequent searching of the art, the Office finds persuasive the applicant's argument that the prior art fails to demonstrated that heparin binding is not required for infection of cardiac tissue by AAV-2. Furthermore, the applicant's representative has argued that the Prior Art does not show a nexus between ablation of heparin binding and preferential infection of heart tissue by

double mutant (R484E and R585E) AAV-2. The examiner has presented teachings which show mutations at R484 and R585 in the AAV-2 capsid proteins, abolish heparin binding (Warrington, Table 5). Furthermore, the cited art demonstrates that mutations R484 and R585 in the AAV-2 capsid drastically reduce or eliminate infection of cells by AAV-2 (Warrington, Table 5). However, the art does not disclose that these particular mutations of AAV-2 capsid proteins permit AAV-2 to retain their ability to infect heart muscle tissue, while eliminating or dramatically reducing their ability to infect other organ tissues, particularly liver. Wild type AAV-2 normally has a high tropism for both heart and liver. The cited art and examiner's reasoning were unable to support the preferential infection of heart muscle tissue by double mutant (R484E and R585E) AAV-2. Therefore, the examiner finds the applicant's method of gene therapy in a heart muscle comprising administration of AAV-2 having two mutations R84E and R585E, each in a different capsid protein to be a non-obvious method.

Therefore, the examiner hereby withdraws the rejection of claims 11, 16-18 and 20 under 35 U.S.C. 103(a) as being obvious over Warrington et al. in view of Bartlett et al. and further in view of Kaplitt et al. and further in view of Wu Xiao.

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Viola Kung on 7/24/2009.

The claims have been amended as follows:

Claim 11. (Currently Amended) A method of gene therapy in a heart muscle tissue of a patient, comprising delivering to the heart muscle tissue of a patient an AAV-2 vector or an AAV-2 particle having a capsid encoded by the AAV-2 vector, wherein the AAV-2 vector ~~carries~~ comprises mutations R484E and R585E according to the numbering based upon VP1 protein, which are in a heparin binding motif of a capsid protein and cause[[s]] a reduced or eliminated heparin binding function, ~~wherein said mutations are R484E and R585E,~~ and wherein ~~amino acids R484 and R585 belong to~~ said mutations are located on different subunits of the capsid protein ~~subunits~~.

Claim 18 is cancelled.

Claims 11, 16-17 and 20 have been renumbered as claims 1-4 according to 37 C.F.R. 1.126 (see MPEP 608.01(j) and 608.01(n).

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

A review of the prosecution history provides rationale for the claim language which is indicated as allowable.

In particular, the examiner has found that the inventors have established a nexus between ablation of heparin binding by AAV-2 capsid protein subunits by mutation of capsid protein at R484 and R485 and subsequent preferential infection of heart muscle tissue by such mutated AAV-2 particles. The art does not make this connection. Therefore, the method of gene therapy to heart muscle tissue would be non-obvious.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Claims 11, 16-17 and 20 are allowed. Claims 1-10, 12-15 and 18 are cancelled.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SDL/ Scott Long
Patent Examiner, Art Unit 1633

/Janet L. Epps-Smith/

Primary Examiner, Art Unit 1633